DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
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Silver Spring, MD 20993-0002

December 10, 2015

Applied Spectral Imaging Ltd.
Ilan Sharon
P.O. Box 4414 (A-109)
Caesarea,30889
Isreal

Re: K140957
Trade/Device Name: GenASIs HiPath IHC Family
Regulation Number: 21 CFR §864.1860
Regulation Name: Immunohistochemistry reagents and kits
Regulatory Class: Class II
Product Code: NQN, NOT
Dated: 12/11/2014
Received: 12/16/2014

Dear Ilan Sharon:

This letter corrects our substantially equivalent letter of January 15, 2015.

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Parts 801 and 809); medical device reporting (reporting of

medical device-related adverse events) (21 CFR 803); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

If you desire specific advice for your device on our labeling regulation (21 CFR Parts 801 and 809), please contact the Division of Industry and Consumer Education at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Industry and Consumer Education at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm.

Sincerely yours,

Reena Philip -S

Reena Philip, Ph.D.
Director
Division of Molecular Genetics and Pathology
Office of *In Vitro* Diagnostics and Radiological Health
Center for Devices and Radiological Health

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: January 31, 2017
See PRA Statement below.

510(k) Number *(if known)*
K140957

Device Name

GenASIs HiPath IHC Family

Indications for Use *(Describe)*

The GenASIs HiPath IHC Family provides image capture, management, analysis, and viewing of specific immunohistochemically stained slides. It is intended for in vitro diagnostic use as an aid to the pathologist in the display, detection, counting, review and classification of tissues and cells of clinical interest based on particular morphology, color, intensity, size, pattern and shape:

1. The GenASIs HiPath IHC Family for HER2 (4B5) is for image capture and analysis applications. This particular system is intended for use as an aid to the pathologist in the detection and semi-quantitative measurement of HER2 protein in formalin-fixed, paraffin-embedded breast cancer tissue. This device is an accessory to Ventana Medical Systems, Inc. PATHWAY® anti-HER2/neu (4B5) Rabbit Monoclonal Primary Antibody. The PATHWAY® anti-HER2/neu (4B5) Rabbit Monoclonal Primary Antibody is indicated for use as an aid in the assessment of breast cancer patients for whom HERCEPTIN® (Trastuzumab) treatment is being considered.

NOTE: The GenASIs HiPath IHC Family for HER2 (4B5) image capture and analysis applications are adjunctive computer-assisted methodologies for the qualified pathologist in the acquisition and semi-quantitative measurement of images from microscope glass slides of breast cancer specimens stained for the presence of HER-2/neu receptor protein. The pathologist should verify agreement with the Image Analysis software application score by reviewing the glass slide under the microscope. The accuracy of the test results depends on the quality of the immuohistochemical staining. It is the responsibility of a qualified pathologist to employ appropriate morphological studies and controls as specified in the instructions for the PATHWAY® anti-HER-2/neu (4B5) Rabbit Monoclonal Primary Antibody assay used to assure the validity of the GenASIs HiPath IHC Family for HER2 (4B5) image capture and analysis scores. The actual correlation of PATHWAY® anti-HER-2/neu (4B5) to clinical outcome has not been established.

2. The GenASIs HiPath IHC Family for PR (1E2) is for image capture and analysis applications. This particular system is intended for use as an aid to the pathologist in the detection and qualitative measurement of progesterone receptor (PR) protein in formalin-fixed, paraffin-embedded breast cancer tissue. This device is an accessory to Ventana Medical Systems, Inc. CONFIRMTM anti-Progesterone Receptor (PR) (1E2) Rabbit Monoclonal Primary Antibody assay. The CONFIRMTM anti-Progesterone Receptor (PR) (1E2) Rabbit Monoclonal Primary Antibody assay is indicated for use as an aid in the assessment of breast cancer patients for whom endocrine treatment is being considered (but is not the sole basis for treatment).

Note: The GenASIs HiPath IHC for PR (1E2) image capture and analysis applications are adjunctive computer-assisted methodologies for the qualified pathologist in the acquisition and qualitative measurement of images from microscope glass slides of breast cancer specimens stained for the presence of PR protein. The pathologist should verify agreement with the Image Analysis software application score by reviewing the glass slide under the microscope. The accuracy of the test results depends on the quality of the immunohistochemical staining. It is the responsibility of a qualified pathologist to employ appropriate morphological studies and controls as specified in the instructions for the CONFIRMTM anti-Progesterone Receptor (PR) (1E2) Rabbit Monoclonal Primary Antibody used to assure the validity of the GenASIs HiPath IHC Family for PR (1E2) image capture and analysis scores. The actual correlation of CONFIRMTM anti-PR antibody to clinical outcome has not been established.

3. The GenASIs HiPath IHC Family for ER (SP1) is for image capture and analysis applications. The particular system is intended for use as an aid to the pathologist in the detection and qualitative measurement of ER (SP1): protein in formalin-fixed, paraffin-embedded breast cancer tissue. This device is an accessory to the Ventana Medical Systems, Inc. CONFIRMTM anti-Estrogen Receptor (ER) (SP1) Rabbit Monoclonal Primary Antibody. The Ventana Medical Systems, Inc. CONFIRMTM anti-Estrogen Receptor (ER) (SP1) Rabbit Monoclonal Primary Antibody is indicated for use as an aid in the assessment of ER status in breast cancer patients (but is not the sole basis for treatment).

Note: The GenASIs HiPath IHC Family for ER (SP1) image capture and analysis applications are adjunctive computer-assisted methodologies for the qualified pathologist in the acquisition and qualitative measurement of images from

microscope glass slides of breast cancer specimens stained for the presence of ER protein. The pathologist should verify agreement with the Image Analysis software application score by reviewing the glass slide under the microscope. The accuracy of the test results depends on the quality of the immuohistochemical staining. It is the responsibility of a qualified pathologist to employ appropriate morphological studies and controls as specified in the instructions for the CONFIRMTM anti-Estrogen Receptor (ER) (SP1) Rabbit Monoclonal Primary Antibody to assure the validity of the GenASIs HiPath IHC Family for ER (SP1) image capture and analysis scores. The actual correlation of CONFIRMTM anti-Estrogen Receptor (ER) (SP1) Rabbit Monoclonal Primary Antibody to clinical outcome has not been established.
4. The GenASIs HiPath IHC Family for Ki67 (30-9) is for image capture and analysis applications. The particular system is intended for use as an aid to the pathologist in the detection and qualitative measurement of Ki67 (30-9): protein in formalin-fixed, paraffin-embedded breast cancer tissue. This device is an accessory to the Ventana Medical Systems, Inc. CONFIRMTM anti-Ki67 (30-9) Rabbit Monoclonal Primary Antibody assay. The Ventana Medical Systems, Inc. CONFIRMTM anti-Ki67 (30-9) assay is indicated for use in assessing the proliferative activity of breast cancer tissue. When used with this assay, the GenASIs HiPath IHC Family for Ki67 (30-9) is indicated for use as an aid in the assessment of Ki-67 status in breast cancer patients (but is not the sole basis for treatment).
Note: The GenASIs HiPath IHC Family for Ki67 (30-9) image capture and analysis applications are adjunctive computer-assisted methodologies for the qualified pathologist in the acquisition and qualitative measurement of images from microscope glass slides of breast cancer specimens stained for the presence of Ki67 protein. The pathologist should verify agreement with the Image Analysis software application score by reviewing the glass slide under the microscope. The accuracy of the test results depends on the quality of the immunohistochemical staining. It is the responsibility of a qualified pathologist to employ appropriate morphological studies and controls as specified in the instructions for the CONFIRMTM anti-Ki67 (30-9) Rabbit Monoclonal Primary Antibody assay to assure the validity of the GenASIs HiPath IHC Family for Ki67 (30-9) image capture and analysis scores. The actual correlation of CONFIRMTM anti-Ki67 (30-9) Rabbit Monoclonal Primary antibody assay to clinical outcome has not been established.

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

PLEASE DO NOT WRITE BELOW THIS LINE – CONTINUE ON A SEPARATE PAGE IF NEEDED.

FOR FDA USE ONLY

Concurrence of Center for Devices and Radiological Health (CDRH) *(Signature)*

This section applies only to requirements of the Paperwork Reduction Act of 1995.

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510(k) Summary

As required by section 807.92(c).
January 15, 2015

A. 510(K) Number

K140957

B. Purpose for Submission

The proposed ASI's GenASIs HiPath IHC Family, including GenASIs HiPath IHC Family for HER2 (4B5), PR (1E2), ER (SP1) and Ki67 (30-9), is an IVD image capture and image analysis score accessory for assist the qualified pathologist in the consistent assessment of protein expression in immunohistochemical stained histological sections from formalin-fixed, paraffin embedded breast cancer tissue.
ASI is hereby preparing this traditional 510(K) submission to show that the proposed ASI's GenASIs HiPath IHC Family is substantially equivalent to the legally marketed predicate devices referred to in paragraph H.

C. Manufacturer and Instrument Name

C.1. Device Name

GenASIs HiPath IHC Family

C.2. Submitter's name

Name: Applied Spectral Imaging Ltd.
2 Ha Carmel St, New Industrial Zone, Yokneam 20691, Israel
Tel: (972) 4 6547567, Fax: (972) 4 6547507

C.3. Submission contact person

Ilan Sharon
P.O.B. 4414 (A-109), Caesarea 30889, Israel
TEL: 972-52-8704904

D. Type of Test or Tests Performed

The GenASIs HiPath IHC Family provides image capture, management, analysis, and viewing of specific immunohistochemically stained slides. It is intended for in vitro diagnostic use as an aid to the pathologist in the display, detection, counting, review and classification of tissues and cells of clinical interest and is intended for use as an aid to the pathologist in the detection and qualitative measurement of the following tests:

1. HER2 protein in formalin-fixed, paraffin-embedded breast cancer tissue. This device is an accessory to Ventana Medical Systems, Inc. PATHWAY® anti-HER2/neu (4B5) Rabbit Monoclonal Primary Antibody. The PATHWAY® anti-HER2/neu (4B5) Rabbit Monoclonal Primary Antibody is indicated for use as an aid in the assessment of breast cancer patients for whom HERCEPTIN® (Trastuzumab) treatment is being considered.

2. Progesterone receptor (PR) protein in formalin-fixed, paraffin-embedded breast cancer tissue. This device is an accessory to Ventana Medical Systems, Inc. CONFIRM™ anti-Progesterone Receptor (PR) (1E2) Rabbit Monoclonal Primary Antibody assay. The CONFIRM™ anti-Progesterone Receptor (PR) (1E2) Rabbit Monoclonal Primary Antibody assay is indicated for use as an aid in the assessment of breast cancer patients for whom endocrine treatment is being considered (but is not the sole basis for treatment).
3. ER (SP1): protein in formalin-fixed, paraffin-embedded breast cancer tissue. This device is an accessory to the Ventana Medical Systems, Inc. CONFIRM™ anti-Estrogen Receptor (ER) (SP1) Rabbit Monoclonal Primary Antibody. The Ventana Medical Systems, Inc. CONFIRM™ anti-Estrogen Receptor (ER) (SP1) Rabbit Monoclonal Primary Antibody is indicated for use as an aid in the assessment of ER status in breast cancer patients (but is not the sole basis for treatment).
4. Ki67 (30-9): protein in formalin-fixed, paraffin-embedded breast cancer tissue. This device is an accessory to the Ventana Medical Systems, Inc. CONFIRM™ anti-Ki67 (30-9) Rabbit Monoclonal Primary Antibody assay. The Ventana Medical Systems, Inc. CONFIRM™ anti-Ki67 (30-9) assay is indicated for use in assessing the proliferative activity of breast cancer tissue. When used with this assay, the GenASIs HiPath IHC Family for Ki67 (30-9) is indicated for use as an aid in the assessment of Ki-67 status in breast cancer patients (but is not the sole basis for treatment).

E. System Descriptions

Device description:

The GenASIs HiPath IHC Family, including software is designed to assist the qualified pathologist in the consistent assessment in inmmohistochemnically stained histologic sections from formalin-fixed, paraffin-embedded breast cancer tissues. The device consists of a slide capture camera, Microscope, computer, monitor, keyboard, mouse, image analysis algorithms for specific immunohistochemical markers, and software with a Graphic User Interface (GUI).
The GenASIs HiPath IHC Family is an intranet-based, end-to-end, digital pathology software solution that allows pathology laboratories, to acquire, manage, view, analyze, share, and report test results of pathology specimens. Using the GenASIs HiPath IHC Family software the pathologist can view captured images, add annotations, make measurements, perform image analysis and generate reports.

Hardware: A camera based acquisition device designed to captures bright-field microscope digital images of formalin-fixed, paraffin-embedded tissues that are suitable for storage and viewing. The device includes a digital slide acquisition camera, X-Y Stage with holder adaptor for loading glass slides on a microscope and a workstation including a computer, keyboard, mouse and monitor.

Software: The GenASIs HiPath IHC Family software is designed to complement the routine workflow of a qualified pathologist in the review of immunohistochemically stained histologic slides. It allows the user to select fields of view (FOVs) in the digital image for analysis and provides quantitative data on these FOVs to assist with interpretation. The software makes no independent interpretations of the data and requires competent human intervention for all steps in the analysis process.

F. Regulatory Information

Device Classification

Product Code:	NQN, NOT
CFR section:	21 CFR §864.1860
Regulation name:	Immunohistrochemistry reagents and kits
Trade Name:	GenASIs HiPath IHC Family
Common Name:	Immunohistrochemistry reagents and kits
Classification:	Class II

G. Intended Use

The GenASIs HiPath IHC Family provides image capture, management, analysis, and viewing of specific immunohistochemically stained slides. It is intended for in vitro diagnostic use as an aid to the pathologist in the display, detection, counting, review and classification of tissues and cells of clinical interest based on particular morphology, color, intensity, size, pattern and shape:

1. The GenASIs HiPath IHC Family for HER2 (4B5) is for image capture and analysis applications. This particular system is intended for use as an aid to the pathologist in the detection and semi-quantitative measurement of HER2 protein in formalin-fixed, paraffin-embedded breast cancer tissue. This device is an accessory to Ventana Medical Systems, Inc. PATHWAY® anti-HER2/neu (4B5) Rabbit Monoclonal Primary Antibody. The PATHWAY® anti-HER2/neu (4B5) Rabbit Monoclonal Primary Antibody is indicated for use as an aid in the assessment of breast cancer patients for whom HERCEPTIN® (Trastuzumab) treatment is being considered.

NOTE: The GenASIs HiPath IHC Family for HER2 (4B5) image capture and analysis applications are adjunctive computer-assisted methodologies for the qualified pathologist in the acquisition and semi-quantitative measurement of images from microscope glass slides of breast cancer specimens stained for the presence of HER-2/neu receptor protein. The pathologist should verify agreement with the Image Analysis software application score by reviewing the glass slide under the microscope. The accuracy of the test results depends on the quality of the immuohistochemical staining. It is the responsibility of a qualified pathologist to employ appropriate morphological studies and controls as specified in the instructions for the PATHWAY® anti-HER-2/neu (4B5) Rabbit Monoclonal Primary Antibody assay used to assure the validity of the GenASIs HiPath IHC Family for HER2 (4B5) image capture and analysis scores. The actual correlation of PATHWAY® anti-HER-2/neu (4B5) to clinical outcome has not been established.

2. The GenASIs HiPath IHC Family for PR (1E2) is for image capture and analysis applications. This particular system is intended for use as an aid to the pathologist in the detection and qualitative measurement of progesterone receptor (PR) protein in formalin-fixed, paraffin-embedded breast cancer tissue. This device is an accessory to Ventana Medical Systems, Inc. CONFIRMTM anti-Progesterone Receptor (PR) (1E2) Rabbit Monoclonal Primary Antibody assay. The CONFIRMTM anti-Progesterone Receptor (PR) (1E2) Rabbit Monoclonal Primary Antibody assay is indicated for use as an aid in the

assessment of breast cancer patients for whom endocrine treatment is being considered (but is not the sole basis for treatment).

Note: The GenASIs HiPath IHC for PR (1E2) image capture and analysis applications are adjunctive computer-assisted methodologies for the qualified pathologist in the acquisition and qualitative measurement of images from microscope glass slides of breast cancer specimens stained for the presence of PR protein. The pathologist should verify agreement with the Image Analysis software application score by reviewing the glass slide under the microscope. The accuracy of the test results depends on the quality of the immunohistochemical staining. It is the responsibility of a qualified pathologist to employ appropriate morphological studies and controls as specified in the instructions for the CONFIRMTM anti-Progesterone Receptor (PR) (1E2) Rabbit Monoclonal Primary Antibody used to assure the validity of the GenASIs HiPath IHC Family for PR (1E2) image capture and analysis scores. The actual correlation of CONFIRMTM anti-PR antibody to clinical outcome has not been established.

3. The GenASIs HiPath IHC Family for ER (SP1) is for image capture and analysis applications. The particular system is intended for use as an aid to the pathologist in the detection and qualitative measurement of ER (SP1): protein in formalin-fixed, paraffin-embedded breast cancer tissue. This device is an accessory to the Ventana Medical Systems, Inc. CONFIRMTM anti-Estrogen Receptor (ER) (SP1) Rabbit Monoclonal Primary Antibody. The Ventana Medical Systems, Inc. CONFIRMTM anti-Estrogen Receptor (ER) (SP1) Rabbit Monoclonal Primary Antibody is indicated for use as an aid in the assessment of ER status in breast cancer patients (but is not the sole basis for treatment).

Note: The GenASIs HiPath IHC Family for ER (SP1) image capture and analysis applications are adjunctive computer-assisted methodologies for the qualified pathologist in the acquisition and qualitative measurement of images from microscope glass slides of breast cancer specimens stained for the presence of ER protein. The pathologist should verify agreement with the Image Analysis software application score by reviewing the glass slide under the microscope. The accuracy of the test results depends on the quality of the immuohistochemical staining. It is the responsibility of a qualified pathologist to employ appropriate morphological studies and controls as specified in the instructions for the CONFIRMTM anti-Estrogen Receptor (ER) (SP1) Rabbit Monoclonal Primary Antibody to assure the validity of the GenASIs HiPath IHC Family for ER (SP1) image capture and analysis scores. The actual correlation of CONFIRMTM anti-Estrogen Receptor (ER) (SP1) Rabbit Monoclonal Primary Antibody to clinical outcome has not been established.

4. The GenASIs HiPath IHC Family for Ki67 (30-9) is for image capture and analysis applications. The particular system is intended for use as an aid to the pathologist in the detection and qualitative measurement of Ki67 (30-9): protein in formalin-fixed, paraffin-embedded breast cancer tissue. This device is an accessory to the Ventana Medical Systems, Inc. CONFIRMTM anti-Ki67 (30-9) Rabbit Monoclonal Primary Antibody assay. The Ventana Medical Systems, Inc. CONFIRMTM anti-Ki67 (30-9) assay is indicated for use in assessing the proliferative activity of breast cancer tissue. When used with this assay, the GenASIs HiPath IHC Family for Ki67 (30-9) is indicated for use as an aid in the assessment of Ki-67 status in breast cancer patients (but is not the sole basis for treatment).

Note: The GenASIs HiPath IHC Family for Ki67 (30-9) image capture and analysis

applications are adjunctive computer-assisted methodologies for the qualified pathologist in the acquisition and qualitative measurement of images from microscope glass slides of breast cancer specimens stained for the presence of Ki67 protein. The pathologist should verify agreement with the Image Analysis software application score by reviewing the glass slide under the microscope. The accuracy of the test results depends on the quality of the immunohistochemical staining. It is the responsibility of a qualified pathologist to employ appropriate morphological studies and controls as specified in the instructions for the CONFIRMTM anti-Ki67 (30-9) Rabbit Monoclonal Primary Antibody assay to assure the validity of the GenASIs HiPath IHC Family for Ki67 (30-9) image capture and analysis scores. The actual correlation of CONFIRMTM anti-Ki67 (30-9) Rabbit Monoclonal Primary antibody assay to clinical outcome has not been established.

H. Substantial Equivalence Information

1. Comparison of Predicate devices:

#	Comparison parameter	Proposed device: ASI GenASIs HiPath IHC Family	Predicate device: Virtuoso™ System
1	**Owner**	**Applied Spectral Imaging Ltd.**	**Ventana Digital Pathology**
2	**Legally distribution clearance No.**	**K……..** Subject to this submission	**K111543 -** Virtuoso™ System for IHC HER2 (4B5) **K111869 -** Virtuoso™ System for IHC PR (1E2) **K130515 -** VirtuosoTM System for IHC ER (SP1) **K111755 -** Virtuoso™ System for IHC Ki67 (30-9)
3	Intended use and indications for use.	The GenASIs HiPath IHC Family provides image capture, management, analysis, and viewing of specific immunohistochemically stained slides. It is intended for in vitro diagnostic use as an aid to the pathologist in the display, detection, counting, review and classification of tissues and cells of clinical interest based on particular morphology, color, intensity, size, pattern and shape: 1. The GenASIs HiPath IHC Family for HER2 (4B5) is for image capture and analysis applications. This particular system is intended for use as an aid to the pathologist in the detection and semi-quantitative measurement of HER2 protein in formalin-fixed, paraffin-embedded breast cancer tissue. This device is an accessory to Ventana Medical Systems, Inc. PATHWAY® anti-HER2/neu (4B5) Rabbit Monoclonal Primary Antibody. The PATHWAY® anti-HER2/neu (4B5) Rabbit Monoclonal Primary Antibody is indicated for use as an aid in the assessment of breast cancer patients for whom HERCEPTIN® (Trastuzumab) treatment is being considered. NOTE: The GenASIs HiPath IHC Family	**K111543 -** Virtuoso™ System for IHC HER2 (4B5) The Virtuoso system provides automatic digital slide creation, management, analysis, and viewing. It is intended for in vitro diagnostic use as an aid to the pathologist in the display, detection, counting, review and classification of tissues and cells of clinical interest based on particular morphology, color, intensity, size, pattern and shape: The Virtuoso™ System for HER2 (4B5) is for digital read and image analysis applications. This particular system is intended for use as an aid to the pathologist in the detection and semi-quantitative measurement of HER2 protein in formalin-fixed, paraffin-embedded normal and neoplastic tissue. This device is an accessory to Ventana Medical Systems, Inc. PATHWAY® anti-HER2/neu (4B5) Rabbit Monoclonal Primary Antibody. The PATHWAY® anti-HER2/neu (4B5) Rabbit Monoclonal Primary Antibody is indicated for use as an aid in the assessment of breast cancer patients for whom HERCEPTIN® (Trastuzumab) treatment is being considered. NOTE: The IHC System for HER2 (4B5) digital read and image analysis applications are adjunctive computer-assisted methodologies for the qualified pathologist in the acquisition and

#	Comparison parameter	Proposed device: ASI GenASIs HiPath IHC Family	Predicate device: Virtuoso™ System
		for HER2 (4B5) image capture and analysis applications are adjunctive computer-assisted methodologies for the qualified pathologist in the acquisition and semi-quantitative measurement of images from microscope glass slides of breast cancer specimens stained for the presence of HER-2/neu receptor protein. The pathologist should verify agreement with the Image Analysis software application score by reviewing the glass slide under the microscope. The accuracy of the test results depends on the quality of the immuohistochemical staining. It is the responsibility of a qualified pathologist to employ appropriate morphological studies and controls as specified in the instructions for the PATHWAY® anti-HER-2/neu (4B5) Rabbit Monoclonal Primary Antibody assay used to assure the validity of the GenASIs HiPath IHC Family for HER2 (4B5) image capture and analysis scores. The actual correlation of PATHWAY® anti-HER-2/neu (4B5) to clinical outcome has not been established.	measurement of images from microscope glass slides of breast cancer specimens stained for the presence of HER-2/neu receptor protein. The pathologist should verify agreement with the Image Analysis software application score. The accuracy of the test results depends on the quality of the immunohistochemical staining. It is the responsibility of a qualified pathologist to employ appropriate morphological studies and controls as specified in the instructions for the PATHWAY® anti-HER-2/neu (4B5) Rabbit Monoclonal Primary Antibody assay used to assure the validity of the iScan System for HER2 4B5 digital read and image analysis scores. The actual correlation of PATHWAY® anti-HER-2/neu (4B5) to clinical outcome has not been established.
		2. The GenASIs HiPath IHC Family for PR (1E2) is for image capture and analysis applications. This particular system is intended for use as an aid to the pathologist in the detection and qualitative measurement of progesterone receptor (PR) protein in formalin-fixed, paraffin-embedded breast cancer tissue. This device is an accessory to Ventana Medical Systems, Inc. CONFIRMTM anti-Progesterone Receptor (PR) (1E2) Rabbit Monoclonal Primary Antibody assay. The CONFIRMTM anti-Progesterone Receptor (PR) (1E2) Rabbit Monoclonal Primary Antibody assay is indicated for use as an aid in the assessment of breast cancer patients for whom endocrine treatment is being considered (but is not the sole basis for treatment). Note: The GenASIs HiPath IHC for PR (1E2) image capture and analysis applications are adjunctive computer-assisted methodologies for the qualified pathologist in the acquisition and qualitative measurement of images from microscope glass slides of breast cancer specimens stained for the presence of PR protein. The	**K111869 -** Virtuoso™ System for IHC PR (1E2) The Virtuoso system provides automatic digital slide creation, management, analysis, and viewing. It is intended for in vitro diagnostic use as an aid to the pathologist in the display, detection, counting, review and classification of tissues and cells of clinical interest based on particular morphology, color, intensity, size, pattern and shape: The Virtuoso™ System for PR (1E2) is for digital read and image analysis applications. This particular system is intended for use as an aid to the pathologist in the detection and semi-quantitative measurement of progesterone receptor (PR) protein in formalin-fixed, paraffin-embedded normal and neoplastic tissue. This device is an accessory to Ventana Medical Systems, Inc. CONFIRM™ anti-Progesterone Receptor (PR) (1E2) Rabbit Monoclonal Primary Antibody assay. The CONFIRM™ anti-Progesterone Receptor (PR) (1E2) Rabbit Monoclonal Primary Antibody assay is indicated for use as an aid in the assessment of breast cancer patients for whom endocrine treatment is being considered (but is not the sole basis for treatment). Note: The IHC PR (1E2) digital read and image analysis applications are adjunctive computer-

#	Comparison parameter	Proposed device: ASI GenASIs HiPath IHC Family	Predicate device: Virtuoso™ System
		pathologist should verify agreement with the Image Analysis software application score by reviewing the glass slide under the microscope. The accuracy of the test results depends on the quality of the immunohistochemical staining. It is the responsibility of a qualified pathologist to employ appropriate morphological studies and controls as specified in the instructions for the CONFIRMTM anti-Progesterone Receptor (PR) (1E2) Rabbit Monoclonal Primary Antibody used to assure the validity of the GenASIs HiPath IHC Family for PR (1E2) image capture and analysis scores. The actual correlation of CONFIRMTM anti-PR antibody to clinical outcome has not been established. 3. The GenASIs HiPath IHC Family for ER (SP1) is for image capture and analysis applications. The particular system is intended for use as an aid to the pathologist in the detection and qualitative measurement of ER (SP1): protein in formalin-fixed, paraffin-embedded breast cancer tissue. This device is an accessory to the Ventana Medical Systems, Inc. CONFIRMTM anti-Estrogen Receptor (ER) (SP1) Rabbit Monoclonal Primary Antibody. The Ventana Medical Systems, Inc. CONFIRMTM anti-Estrogen Receptor (ER) (SP1) Rabbit Monoclonal Primary Antibody is indicated for use as an aid in the assessment of ER status in breast cancer patients (but is not the sole basis for treatment). Note: The GenASIs HiPath IHC Family for ER (SP1) image capture and analysis applications are adjunctive computer-assisted methodologies for the qualified pathologist in the acquisition and qualitative measurement of images from microscope glass slides of breast cancer specimens stained for the presence of ER protein. The pathologist should verify agreement with the Image Analysis software application score by reviewing the glass slide under the microscope. The accuracy of the test results depends on the quality of the immuohistochemical staining. It is the responsibility of a qualified pathologist to employ appropriate morphological studies and controls as specified in the instructions	assisted methodologies for the qualified pathologist in the acquisition and measurement of images from microscope glass slides of breast cancer specimens stained for the presence of PR protein. The pathologist should verify agreement with the Image Analysis software application score. The accuracy of the test results depends on the quality of the immunohistochemical staining. It is the responsibility of a qualified pathologist to employ appropriate morphological studies and controls as specified in the instructions for the CONFIRM™ anti-Progesterone Receptor (PR) (1E2) Rabbit Monoclonal Primary Antibody used to assure the validity of the Virtuoso System for PR (1E2) digital read and image analysis scores. The actual correlation of CONFIRM™ anti-PR antibody to clinical outcome has not been established. **K130515 -** VirtuosoTM System for IHC ER (SP1) The Virtuoso system provides automated digital slide creation, management, analysis, and viewing. It is intended for in vitro diagnostic use as an aid to the pathologist in the display, detection, counting, review and classification of tissues and cells of clinical interest based on particular morphology, color, intensity, size, pattern and shape. The Virtuoso™ System for IHC ER (SP1) is for digital read and image analysis applications. This particular Virtuoso system is intended for use as an aid to the pathologist in the detection and semi-quantitative measurement of estrogen receptor (ER) protein in formalin-fixed, paraffin-embedded neoplastic tissue. This device is an accessory to Ventana Medical Systems, Inc. CONFIRM™ anti-Estrogen Receptor (ER) (SF1) Rabbit Monoclonal Primary Antibody assay. The CONFIRM™ anti- ER (SF1) Rabbit Monoclonal Primary Antibody assay is indicated for use as an aid in the assessment of breast cancer patients for whom endocrine treatment is being considered (but is not the sole basis for treatment). Note: The IHC ER (SPI) Digital Read and Image Analysis applications are adjunctive computer-assisted methodologies for the qualified pathologist in the acquisition and measurement of images from microscope glass slides of breast cancer specimens stained for the presence of ER protein. The pathologist should verify agreement with the Image Analysis software application

#	Comparison parameter	Proposed device: ASI GenASIs HiPath IHC Family	Predicate device: Virtuoso™ System
		for the CONFIRMTM anti-Estrogen Receptor (ER) (SP1) Rabbit Monoclonal Primary Antibody to assure the validity of the GenASIs HiPath IHC Family for ER (SP1) image capture and analysis scores. The actual correlation of CONFIRMTM anti-Estrogen Receptor (ER) (SP1) Rabbit Monoclonal Primary Antibody to clinical outcome has not been established. 4. The GenASIs HiPath IHC Family for Ki67 (30-9) is for image capture and analysis applications. The particular system is intended for use as an aid to the pathologist in the detection and qualitative measurement of Ki67 (30-9): protein in formalin-fixed, paraffin-embedded breast cancer tissue. This device is an accessory to the Ventana Medical Systems, Inc. CONFIRMTM anti-Ki67 (30-9) Rabbit Monoclonal Primary Antibody assay. The Ventana Medical Systems, Inc. CONFIRMTM anti-Ki67 (30-9) assay is indicated for use in assessing the proliferative activity of breast cancer tissue. When used with this assay, the GenASIs HiPath IHC Family for Ki67 (30-9) is indicated for use as an aid in the assessment of Ki-67 status in breast cancer patients (but is not the sole basis for treatment). Note: The GenASIs HiPath IHC Family for Ki67 (30-9) image capture and analysis applications are adjunctive computer-assisted methodologies for the qualified pathologist in the acquisition and qualitative measurement of images from microscope glass slides of breast cancer specimens stained for the presence of Ki67 protein. The pathologist should verify agreement with the Image Analysis software application score by reviewing the glass slide under the microscope. The accuracy of the test results depends on the quality of the immunohistochemical staining. It is the responsibility of a qualified pathologist to employ appropriate morphological studies and controls as specified in the instructions for the CONFIRMTM anti-Ki67 (30-9) Rabbit Monoclonal Primary Antibody assay to assure the validity of the GenASIs HiPath IHC Family for Ki67 (30-9) image capture and analysis scores. The actual correlation of CONFIRMTM anti-Ki67 (30-9) Rabbit	score. The accuracy of the test results depends on the quality of the immuohistochemical staining. It is the responsibility of a qualified pathologist to employ appropriate morphological studies and controls as specified in the instructions for the CONPIRM™ anti-Estrogen Receptor (ER) (SP3) Rabbit Monoclonal Primary Antibody used to assure the validity of the Virtuoso System for IHC ER Digital Read and Image Analysis scores. The actual correlation of CONFIRM™ anti-Estrogen Receptor (ER)(SPI) Rabbit Monoclonal Antibody to clinical outcome has not been established. **K111755 -** Virtuoso™ System for IHC Ki67 (30-9) The Virtuoso system provides automatic digital slide creation, management, analysis, and viewing. It is intended for in vitro diagnostic use as an aid to the pathologist in the display, detection, counting, review and classification of tissues and cells of clinical interest based on particular morphology, color, intensity, size, pattern and shape: The Virtuoso™ System for Ki67 (30-9) is for digital read and image analysis applications. The particular system is intended for use as an aid to the pathologist in the detection and semi-quantitative measurement of Ki67 (30-9): protein in formalin-fixed, paraffin-embedded normal and neoplastic tissue. This device is an accessory to the Ventana Medical Systems, Inc. CONFIRM™ anti-Ki67 (30-9) Rabbit Monoclonal Primary Antibody assay. The Ventana Medical Systems, Inc. CONFIRM™ anti-Ki67 (30-9) assay is indicated for use in assessing the proliferative activity of normal and neoplastic breast tissue. When used with this assay, the Virtuoso™ System for Ki67 (30-9) is indicated for use as an aid in the assessment of Ki-67 status in breast cancer patients (but is not the sole basis for treatment). Note: The IHC Family for Ki67 (30-9) digital read and image analysis applications are adjunctive computer-assisted methodologies for the qualified pathologist in the acquisition and measurement of images from microscope glass slides of breast cancer specimens stained for the presence of Ki67 protein. The pathologist should verify agreement with the Image Analysis software application score. The accuracy of the test results depends on the quality of the inunmohistochemnical staining. It is the

#	Comparison parameter	Proposed device: ASI GenASIs HiPath IHC Family	Predicate device: Virtuoso™ System
		Monoclonal Primary antibody assay to clinical outcome has not been established	responsibility of a qualified pathologist to employ appropriate morphological studies and controls as specified in the instructions for the CONFIRM™ anti-Ki67 (30-9) Rabbit Monoclonal Primary Antibody assay to assure the validity of the Virtuoso™ System for Ki67 (30-9) digital read and image analysis scores. The actual correlation of CONFIRM™ anti-Ki67 (30-9) Rabbit Monoclonal Primary antibody assay to clinical outcome has not been established.
4	Application: IHC HER2 (4B5)	Detection and semi-quantitative measurement of HER2 protein in formalin-fixed, paraffin-embedded breast cancer tissue	Detection and semi-quantitative measurement of HER2 protein in formalin-fixed, paraffin-embedded normal and neoplastic tissue
5	Application: IHC PR (1E2)	Detection and qualitative measurement of progesterone receptor (PR) protein in formalin-fixed, paraffin-embedded breast cancer tissue.	Detection and semi-quantitative measurement of progesterone receptor (PR) protein in formalin-fixed, paraffin-embedded normal and neoplastic tissue.
6	Application: IHC ER (SP1)	Detection and qualitative measurement of Estrogen Receptor (ER) protein in formalin-fixed, paraffin-embedded breast cancer tissue.	Detection and semi-quantitative measurement of Estrogen Receptor (ER) protein in formalin-fixed, paraffin-embedded normal and neoplastic tissue.
7	Application: IHC Ki67 (30-9)	Detection and qualitative measurement of Ki67 (30-9): protein in formalin-fixed, paraffin-embedded breast cancer tissue.	Detection and semi-quantitative measurement of Ki67 (30-9): protein in formalin-fixed, paraffin-embedded normal and neoplastic tissue.
8	Specimen Identification	By the pathologist, according the single slide label.	Identified by slide label or barcode.
9	Calibration	Camera White Balance	Tests must be run with nine custom slides calibrated for the module which can be obtained from the sponsor.
10	Quality Control	Performed by the operator as part of the standard operation procedures using slides with sub-optimal images.	Performed by the operator before releasing the images to the pathologist for review. Slides with sub-optimal images will be rescanned
11	Slide acquisition/ Capture	CCD high resolution color camera and racks for loading the glass slides. Images to be processed selected via microscope's eyepiece.	Digital slide bright field scanner (Ventana iScan) and racks for loading glass slides. Images to be processed selected from the screen digital read image.
12	Device Components	Microscope, CCD color camera, PC, keyboard, Mouse, Color Monitor, X-Y stage and rack for loading 1 glass slide.	Digital slide scanner, PC, keyboard, Mouse, color Monitor, racks for loading up to 160 glass slides.

2. Substantial Equivalence discussion

Similarities:

Intended Use:

The proposed GenASIs HiPath IHC Family and the legally cleared Virtuoso™ Systems (K111543, K111869, K130515 and K111755) have the same intended use and indications for use for the following: Acquisition, image capture, management, analysis, and viewing. The proposed GenASIs HiPath IHC Family and the legally cleared Virtuoso™ Systems are intended for in vitro diagnostic use as an aid to the pathologist in the display, detection, counting, review and classification of tissues and cells of clinical interest based on particular morphology, color, intensity, size, pattern and shape.

The proposed GenASIs HiPath IHC Family and the legally cleared Virtuoso™ Systems are indicated as an aid to pathologists in the assessment of HER2, PR, ER and Ki67 (30-9) status in breast cancer patients.

Performance:

The proposed GenASIs HiPath IHC Family and the legally cleared Virtuoso™ Systems are designed for the same IVD applications (H1 sections 3 – 6) using similar hardware and software components and similar analysis tools, the pathologist has to select the ROI for the scoring algorithm (H1 sections 7, 8) and calibration and quality control has to be performed to make sure that scoring results are stable (Table 4.3 sections 10, 11).

Technology:

The proposed GenASIs HiPath IHC Family and the legally cleared Virtuoso™ Systems are using similar hardware and software components, designed to complement the routine workflow of a qualified pathologist in the review of IHC stained histological slides (H1 section 12).

Differences:

Intended Use:

No difference

Performance:

1. The legally cleared Virtuoso™ Systems are using slide scanner for generating the digital slide while the proposed GenASIs HiPath IHC Family is using a color camera to capture and convert the microscope's image to a digital image.
2. Images to be processed selected from Vituoso's screen digital read image, while in the proposed GenASIs HiPath IHC Family images for processing are selected via microscope's eyepiece (H1 section 11).
3. Calibration and quality control processes are different in both systems (H1 sections 10, 11).
4. Legally cleared Virtuoso™ Systems are designed for multi slide automatic loading, slide label or automatic barcode for specimen identification method must be used while the GenASIs HiPath IHC Family glass slide loading is manual and the pathologist is responsible for the slide identification (H1 section 9).

The effectiveness of the proposed GenASIs HiPath IHC Family calibration and quality control processes were verified and validated during the clinical studies.

Technology:
1. The legally cleared Virtuoso™ Systems use a slide scanner for generating the digital slide while the proposed GenASIs HiPath IHC Family use a color camera to capture and convert the microscope's image to a digital image.
2. Acquisition control software and illumination light sources are different and optimized to the acquisition flow and process (H1, sections 10 – 11).
3. The Virtuoso™ System have additional hardware components; automatic multi slides loader, slides identifier and slide scanner, as opposed to the proposed GenASIs HiPath IHC Family that is using a magnifying microscope for manual slide capture (H1, section 12).

I. Special Control/ Guidance Document Referenced (if applicable)

The following Special Control and guidance documents are used in the preparation of the 510(K) submission:

1. Guidance for Industry "Guidance for Submission of Immunohistochemistry Applications to the FDA", dated June 3 1998.

2. CLSI I/LA28-A2Q:2009 - uality assurance for design control and implementation of immunohistochemistry assays; approved guidelines-second edition. (InVitro Diagnostics).

3. Guidance for Industry and FDA Staff: "Statistical Guidance on Reporting Results from Studies Evaluating Diagnostic Tests"; March 2007.

4. "Guidance for the Content of Premarket Submission for Software Contained in Medical Device", CDRH, May 2005.

5. Guidance for Industry, Clinical Investigators, Institutional Review Boards and Food and Drug Administration Staff, Doc. 1776 dated November 2013

J. Performance Characteristics

The following information of the device performance characteristics are based on ASI testing and experiments, using the following Ventana Medical Systems, Inc probe kits:

- PATHWAY® anti-HER2/neu (4B5) Rabbit Monoclonal Primary Antibody
- CONFIRM™ anti-Progesterone Receptor (PR) (1E2) Rabbit Monoclonal Primary Antibody assay
- CONFIRM™ anti-Estrogen Receptor (ER) (SP1) Rabbit Monoclonal Primary Antibody
- CONFIRM™ anti-Ki67 (30-9) Rabbit Monoclonal Primary antibody assay

The user must use the staining process described in Ventana's user instructions for the above mentioned assay kits. Additionally, clinical sensitivity, clinical specificity and clinical cut-off are also related to the above mentioned assay kits (as per user instructions).

The operators shall be aware of limitations derived from the following performance characteristics:

a. Analytical Performance:

The clinical studies were based on comparison to the measures of agreement test of conventional manual evaluation through the microscope eyepieces, performed by

pathologist that followed the recommendations of the Ventana user insertions for the different panel antibodies and test analysis performed with the proposed GenASIs HiPath IHC Family system, using the same stained slides.

The comparison study was conducted in three clinical sites, by three different pathologists, according to Applied Spectral Imaging's protocol.
The study included a total of:

- HER2/neu (4B5) - 357 stained samples.
- PR (1E2) - 385 stained samples.
- ER (SP1) - 427 stained samples
- Ki67 (30-9) - 373 stained samples

The agreement rates of the comparison between manual and GenASIs HiPath IHC Family system statistical test results when pooling all three sites tests are:

HER2/neu (4B5)

Pooled Results; Frequency distribution of agreement of Manual versus GenASIs HiPath IHC Family:

		Manual analysis		
		Negative (0, 1+)	Positive (2+, 3+)	Total
GenASIs HiPath IHC analysis	Negative (0, 1+)	185	5	190
	Positive (2+, 3+)	4	163	167
	Total	189	168	357
Overall Agreement		97%		
Positive Agreement		98%		
Negative Agreement		97%		

PR (1E2)

Pooled Results; Frequency distribution of agreement of Manual versus GenASIs HiPath IHC Family:

		Manual analysis		
		Negative (<1%)	Positive (≥1%)	Total
GenASIs HiPath IHC analysis	Negative (<1%)	161	1	162
	Positive (≥1%)	3	220	223
	Total	164	221	385
Overall Agreement		99%		
Positive Agreement		98%		
Negative Agreement		100%		

ER (SP1)

Pooled Results; Frequency distribution of agreement of Manual versus GenASIs HiPath IHC Family:

		Manual analysis		
		Negative (<1%)	Positive (≥1%)	Total
GenASIs HiPath IHC analysis	Negative (<1%)	151	1	152
	Positive (≥1%)	1	274	275
	Total	152	275	427
Overall Agreement		100%		
Positive Agreement		99%		
Negative Agreement		100%		

Ki67 (30-9)

Pooled Results; Frequency distribution of agreement of Manual versus GenASIs HiPath IHC Family:

		Manual analysis		
		Negative (≤10%)	Positive (>10%)	Total
GenASIs HiPath IHC analysis	Negative (≤10%)	132	6	138
	Positive (>10%)	10	225	235
	Total	142	231	373
Overall Agreement		96%		
Positive Agreement		93%		
Negative Agreement		97%		

b. Precision/Reproducibility:

Repeatability and reproducibility (R&R) studies were conducted to evaluate the variation in the performance of the automatic system between different runs of the same system and same day, between days of the same system and between systems located on different sites. Separate tests were performed for HER2/neu, ER, PR and Ki-67. For each antibody, forty (40) slides were selected, aiming to cover the samples result categories of the intended population.

The one hundred and sixty (160) slides were selected from a known pool as follows:

- For ER & PR slides were selected from positive, negative and around-cutoff slides to cover the entire clinically relevant range
- For Ki67 slides were selected from positive, negative slides to cover the entire clinically relevant range
- For HER2/neu slides were selected from the 4 classes of 0,1+,2+,3+.

All slides were labeled by slide index and antibody type.
Slides were evaluated by three independent pathologists and than were repeatedly evaluated

by the GenASIs HiPath IHC family device.
A minimal washout time between manual and GenASIs HiPath analysis was 7 days.
The precision of manual and system results is reported separately.

The following factors were used for testing GenASIs HighPath family precision:

i) Run – Each slide is re-evaluated three times on a same system and on a same day.

ii) Day - Each slide is re-evaluated three times on non-consecutive days (at least 5 days apart) on a same system.

iii) System - Each slide is re-evaluated three times using different systems (at least 7 days apart).

HER2/neu (4B5)

The study includes forty (40) sample slides for each antibody, which represent the range of the intended use.

The R&R agreements for positive and negative sample slides analysis were:

Between-Run, Within-Day, Within-System:

	Average Positive Agreement (2+, 3+)	Average Negative Agreement (0, 1+)
Run 1 vs Run 2	97.6%	97.5%
Run 1 vs Run 3	95.0%	95.0%
Run 2 vs Run 3	97.6%	97.5%

Between-Day, Within-System:

	Average Positive Agreement (2+, 3+)	Average Negative Agreement (0, 1+)
Day 1 vs Day 2	100%	100%
Day 1 vs Day 3	97.6%	97.5%
Day 2 vs Day 3	97.6%	97.5%

Between-Systems:

	Average Positive Agreement (2+, 3+)	Average Negative Agreement (0, 1+)
Sys 1 vs Syst 2	97.6%	97.5%
Sys 1 vs Sys 3	97.5%	97.6%
Sys 2 vs Sys 3	95.2%	95.2%

PR (1E2)

The study include forty (40) sample slides for each antibody, which represent the range of the intended use.
The R&R agreements for positive and negative sample slides analysis were:

Between-Run, Within-Day, Within-System:

	Average Positive Agreement (≥ 1%)	Average Negative Agreement (<1%)
Run 1 vs Run 2	100.0%	100.0%
Run 1 vs Run 3	100.0%	100.0%
Run 2 vs Run 3	100.0%	100.0%

Between-Day, Within-System:

	Average Positive Agreement (≥ 1%)	Average Negative Agreement (<1%)
Day 1 vs Day 2	97.9%	97.1%
Day 1 vs Day 3	97.9%	97.1%
Day 2 vs Day 3	95.8%	93.8%

Between-Systems:

	Average Positive Agreement (≥ 1%)	Average Negative Agreement (<1%)
Sys 1 vs Sys 2	97.9%	97.1%
Sys 1 vs Sys 3	97.9%	97.1%
Sys 2 vs Sys 3	100.0%	100.0%

ER (SP1)

The study include forty (40) sample slides for each antibody, which represent the range of the intended use.

The R&R agreements for positive and negative sample slides analysis were:

Between-Run, Within-Day, Within-System:

	Average Positive Agreement (≥ 1%)	Average Negative Agreement (<1%)
Run 1 vs Run 2	100.0%	100.0%
Run 1 vs Run 3	100.0%	100.0%
Run 2 vs Run 3	100.0%	100.0%

Between-Day, Within-System:

	Average Positive Agreement (≥ 1%)	Average Negative Agreement (<1%)
Day 1 vs Day 2	100.0%	100.0%
Day 1 vs Day 3	100.0%	100.0%
Day 2 vs Day 3	100.0%	100.0%

Between-Systems:

	Average Positive Agreement (≥ 1%)	Average Negative Agreement (<1%)
Sys 1 vs Sys 2	100.0%	100.0%
Sys 1 vs Sys 3	100.0%	100.0%
Sys 2 vs Sys 3	100.0%	100.0%

Ki67 (30-9)

The study includes forty (40) sample slides for each antibody, which represent the range of the intended use.
The R&R agreement for positive and negative sample slides analysis was:

Between-Run, Within-Day, Within-System:

	Average Positive Agreement (>10%)	Average Negative Agreement (≤10%)
Run 1 vs Run 2	97.9%	97.1%
Run 1 vs Run 3	89.4%	84.9%
Run 2 vs Run 3	91.3%	88.2%

Between-Day, Within-System:

	Average Positive Agreement (>10%)	Average Negative Agreement (≤10%)
Day 1 vs Day 2	95.8%	93.8%
Day 1 vs Day 3	95.8%	93.8%
Day 2 vs Day 3	95.8%	93.8%

Between-Systems:

	Average Positive Agreement (>10%)	Average Negative Agreement (≤10%)
Sys 1 vs Sys 2	95.8%	93.8%
Sys 1 vs Sys 3	97.9%	97.1%
Sys 2 vs Sys 3	97.9%	97.1%

c. Linearity

Not applicable

d. Carryover:

Not applicable

e. Interfering Substances:

Not applicable

3. Other Supportive Instrument Performance Data Not Covered Above:

Not applicable

K. Proposed Labeling

Labeling was prepared in accordance with the requirements of 21 CFR Part 809.10.

L. Conclusion

Based on the above, it is Applied Spectral Imaging's opinion that the proposed GenASIs HiPath IHC Family is substantially equivalent in terms of design, principles, and performance characteristics and is shown to be safe & effective for its intended use.